

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

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| Applicant's or agent's file reference see form PCT/ISA/220 | | Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet) |
| International application No. PCT/EP2004/000065 | International filing date (day/month/year) 08.01.2004 | Priority date (day/month/year) 08.01.2003 |
| International Patent Classification (IPC) or both national classification and IPC C12N15/90, C12N15/63, C12N5/10, A01K67/00 | | |
| Applicant ARTEMIS PHARMACEUTICALS GMBH | | |

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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| Name and mailing address of the ISA:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Herrmann, K Telephone No. +49 89 2399-2670 |
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP04/00065

Citations

The documents are numbered as in the International Search Report (ISR), i.e. D1 and D6 correspond to the first and the last document of the search report, respectively.

The application as filed contains a sequence listing consisting of 23 pages (9 sequences).

- 1 Claims 10 and 13 fail to comply with the requirements of Art. 6 PCT (clarity) to such an extent that a meaningful search and examination could not be carried out (Art. 17(2)(a)(ii) PCT, Rule 66.1(e) PCT, also cf. PCT Guidelines VI-8.4, last sentence). Claim 10 is directed to a product, namely a targeting vector as defined in claims 1-8. Method claim 13 refers to modifying an ES cell as defined in claims 1-9. However, claims 1-9 are directed to a method for generating transgenic eukaryotic cells and not to any products.
 - 2 Claims 1-9, 12-14 and 16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT (*in vivo* treatment or diagnostic methods practiced on the human or animal body). Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

Re ITEM V (Novelty, inventive step, industrial applicability)

- 1 Novelty and inventive step (Art. 33(2) and (3) PCT)
 - 1.1 The subject-matter of claims 1-9, 11, 12 and 14-16 does not meet the requirements of Art. 33(2) and 33(3) PCT.
 - 1.2 D1 (WO9953017) and D2 (WO0238613) disclose a method according to

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independent claim 1. The subject-matter of independent claim 1 can thus not be regarded as novel.

- 1.3 A positive international preliminary examination report (IPER) could only be established if claims 2-9, 11, 12 and 14-16 refer to a claim which can be regarded as novel and inventive.
- 1.4 Similar results have been disclosed in D3 (WO02098217), D4 (Dacquin et al.) and D5 (Moses et al.) which therefore also deprive novelty of claims 1-9, 11, 12 and 14-16 (Art. 33(2) and (3) PCT).
- 1.5 It should be noted that expressions like "preferably" (e.g. claim 3) have no limiting effect on the scope of a claim; that is to say the feature following any such expression is to be regarded as entirely optional (PCT Guidelines III-4.6).
- 1.6 The terms "DNA sequence which can be converted into..." (e.g. claim 1), "homologous" (e.g. claim 6) and "derived from" (e.g. claim 6) are vague and further jeopardize the novelty of said claims.

2 Industrial application (Art. 33(4) PCT)

Claims 11 and 15 meet the criteria as set forth by Art. 33(4) PCT.

Re ITEM VI

Certain published documents (Rule 70.10)

| Application No Patent No | Publication date (day/month/year) | Filing date (day/month/year) | Priority date (valid claim) (day/month/year) |
|-----------------------------|--------------------------------------|---------------------------------|---|
| WO03020743 | 13.03.03 | 05.09.02 | 05.09.01 |

Said document has been published after but filed before the claimed priority date of the present application and does therefore not constitute prior art in the meaning of Rule 64(1)(b) PCT. It will, however, become of relevance for the novelty of the claimed subject-matter during regional phase examination.

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Re ITEM VIII (Certain observations on the international application)

Claims 1-5, 7-9, 11, 12, 14 and 16 also encompass human embryonic stem cells or the use thereof. This subject-matter may be contrary to morality in certain PCT member states (cf. e.g. Art. 53(a) of the EPC).

Claim 15 also encompasses transgenic human beings. This subject-matter is contrary to morality in certain PCT member states (cf. e.g. Art. 53(a) of the EPC).

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Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

see separate sheet

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Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
- claims Nos. 10, 13 and with respect to industrial application claims 1-9, 12-14 and 16 because:
- the said international application, or the said claims Nos. 1-9, 12-14 and 16 with respect to industrial examination (specify):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 10 and 13 are so unclear that no meaningful opinion could be formed (specify):
see separate sheet
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the whole application or for said claims Nos.
- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
the written form has not been furnished
 does not comply with the standard
the computer readable form has not been furnished
 does not comply with the standard
- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|-------------------------------|------|--------|--------------------|
| Novelty (N) | Yes: | Claims | |
| | No: | Claims | 1-9, 11, 12, 14-16 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-9, 11, 12, 14-16 |
| Industrial applicability (IA) | Yes: | Claims | 11, 15 |
| | No: | Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

- 1. Certain published documents (Rules 43bis.1 and 70.10)**
and / or
- 2. Non-written disclosures (Rules 43bis.1 and 70.9)**

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet